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| 09/363,748 | 07/30/1999 | CAROL WATKINS | 108137.701 | 8501 |

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| EXAMINER |
|---|
| CRANE, LAWRENCE E |

| ART UNIT | PAPER NUMBER |
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| 1623 | 25 |

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Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. 09/363,748 | Applicant(s) Watkins et al. | |
|---|---|---|---|
| | Examiner L. E. Crane | Group Art Unit 1623 | |

***- THE MAILING DATE of this communication appears on the cover sheet beneath the correspondence address -***

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE --3-- MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be filed after six months from the date of this communication.
- If the prior for reply specified above is less that thirty (30) days, a reply within the statutory minimum of thirty days will be considered timely.
- If NO period for reply is specified above, such period shall ,by default, expire SIX (6) MONTHS from the date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 USC §133).

## Status

[X] Responsive to communication(s) filed on -08/01/02 (amdt E)-.
[X] This action is **FINAL.**
[] Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 11; 453 O.G. 213.

## Disposition of Claims

[X] Claims --39 and 41-50-- are pending in the application. Claim -40- has been cancelled.
Of the above claim --46-49-- is withdrawn from consideration.
[] Claim(s) --[]-- is/are allowed.
[X] Claims --39, 41-45 and 50-- are rejected.
[] Claim(s) --[]-- is/are objected to.
[] Claim(s) --[]-- are subject to restriction or election requirement.

## Application Papers

[] See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
[] The proposed drawing correction, filed on -[]- is [] approved [] disapproved.
[] The drawing(s) filed on -[]- is/are objected to by the Examiner.
[] The specification is objected to by the Examiner.
[] The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119(a)-(d)

[] Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119 (a)-(d).
[] All [] Some* [] None of the CERTIFIED copies of the priority documents have been
[] received.
[] received in Application No. (Series Code/Serial Number) -[]-.
[] received in the national stage application from the International Bureau (PCT Rule 17.2(a)).
* Certified copies not received: -[]-.

## Attachment(s)

[] Information Disclosure Statement(s), PTO-1449, Paper No(s). --[]--
[] Notice of Reference(s) Cited, PTO-892
[] Notice of Draftsperson's Patent Drawing Review, PTO-948
[] Interview Summary, PTO-413
[] Notice of Informal Patent Application, PTO-152
[] Other: -[]-.

Claim **40** has been cancelled, claims **39, 41-42, 44-47 and 49** have been amended, pages 6 and 12 of the disclosure have been amended, and no new claims have been added as per the amendment filed August 1, 2002.

Claims **39 and 41-50** remain in the case.

Claims **46-49** are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the "other" compounds listed in the noted claim are not all found in the cancelled claims 30-31 or in any other claims now cancelled. In addition, the newly added term "at least one additional [compound]" in each of claims **46-49** extends this subject matter even further outside the bounds of the originally presented invention and would require additional search and consideration.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly claims **46-49** have been withdrawn from consideration as being directed to a non-elected invention. See 37 C.F.R. §1.142(b) and MPEP §821.03.

Applicant's arguments filed August 1, 2002 have been fully considered but they are not persuasive.

Applicant argues that withdrawal of claim **47** is inappropriate because there would be minimal search burden and that the invention is not patentably distinct. Examiner respectfully disagrees, and notes that claims **46, 48 and 49** have also been withdrawn herein as having the same problem. The problem is that applicant received a search on the

merits of the claims as originally submitted, a search which did not take into consideration the possibility of one or more additional active ingredients. This is patentably distinct subject matter and would require a separate search.

Claims **39, 41-45 and 50** remain under examination.

Claims **39, 41-45 and 50** are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Inspection of the instant disclosure reveals no specific test data to support the generic limitations ("a neurological disorder," "a memory disorder," "memory disorder associated with aging") directed to the treatment of a disease condition or conditions, by the administration of uridine, cytidine, mixtures of uridine and cytidine, or any other uridine- or cytidine-containing binary or higher order mixtures of active or prodrug/precursor ingredients. For example, the noted claims read on the treatment of senile dementia, HIV-related dementia, and Alzheimer's disease, but the instant disclosure fails to provide any evidence that the instant method is effective in the treatment of any one of these disease conditions. Therefore, the instant disclosed exemplifications relevant to the instant claims are deemed to be entirely prospective and therefore lacking any enabling effect.

Applicant's arguments filed August 1, 2002 have been fully considered but they are not persuasive.

Applicant cites the MPEP to the effect that a single working example is enough to enable a medicinal method of treating claim, citing

"example 2 and associated Figures 2 and 4." However, inspection of the instant claims indicates that claim **39** is the only directed to increasing levels of brain cytidine by administration of uridine "to a human [host] in need thereof," but fails to define the medicinal "need" and therefore is not a complete method of treating claim. Therefore, while applicant may accurately allege that there is "a working example" in the disclosure, said example or examples fail to enable the claim because the claim is a medicinal method of treating, not a method of nutritional supplementation. Applicant has simply not provided any relevant data to enable any medicinal method of treatment claim, including the suggestion by claim **45** that administration of uridine produces an effective treatment of any cerebral disease condition, including memory loss as a consequence of aging. If such data is available, applicant is encouraged to refile the instant case with the added data incorporated therein (CIP). Examiner also notes that nearly all of the the remaining examples are stated in the present tense and lack supporting experimental results, clear indications that these examples are entirely prospective. Applicant is respectfully requested to review *Brenner v. Manson*, 148 USPQ 689 (S. Ct. 1966), which stands in part for the view that a patent is granted for explorations already accomplished and is "... not a hunting license." Additionally, applicant is reminded that it is well known and established that "law requires that disclosure in an application shall inform those skilled in the art how to use appellant's alleged discovery, not how to find out how to use it for themselves." *In re Gardner et al.*, 166 USPQ 138 (CCPA 1970). Therefore, the instant grounds of rejection has been maintained for the reasons noted.

Claims **39 and 41-45 and 50** are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in

the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

There is no specific exemplification found the instant disclosure which provides guidance concerning the effect of administering "uridine" at the rate of "less than 300 mg/day" on the treatment of any brain or neurological (nervous system) disease condition including any specific memory disorder. Therefore, the newly introduced limitation in claim **39** wherein the administration of uridine is limited to the rate of " ... less than 300 mg/day" represents new matter and its deletion is therefore respectfully requested.

Applicant's arguments with respect to claims **39-50** have been considered but are moot in view of the new grounds of rejection. The new grounds of rejection was necessitated by applicant's introduction of a new dosage limitation into claim **39**.

Claims **39, 41-45 and 50** are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim **39** appears to be an incomplete method of treating claim because it fails to include a specific disease condition to be treated. This means that the limitations added in claims **41, 42 and 45** lack proper antecedent basis in claim **39**, and/or that claims **41, 42 and 45** are entirely superfluous because they fail to further limit any patentable feature of independent claim **39**.

Applicant's arguments filed August 1, 2002 have been fully considered but they are not persuasive.

Applicant alleges that there is a long unmet need to find a way to increase cytidine level in the brain. While this may be the case from a nutritional point of view, this does not render the instant claim complete as a medicinal method of treating claim. In addition, the amendments of claims **41, 42 and 45** do not overcome this problem, but said amendments do make it clear that said claims lack proper antecedent basis in claim **39** and also that said claims fail to further limit any patentable feature of claim **39**. For these reasons the instant grounds of rejection has been maintained.

In claim **39**, the term " uridine or a precursor thereof " is directed to subject matter (or a precursor thereof) which as a functional term directed to chemical species lacks adequately defined metes and bounds. The same problem reoccurs in claim **50**, and a similar problem ("uridine or its precursor") occurs in claims **43-44**.

Applicant's arguments filed August 1, 2002 have been fully considered but they are not persuasive.

Applicant cites the disclosure's definition in support of the term "uridine precursor." The quoted definition, to be effective in the suggested role, must itself meet the requirements of the cited statute. Unfortunately, the included term "e.g." (aka "for example") is per se indefinite and therefore the quoted definition is deemed to suffer from the same problem (indefiniteness as to metes and bounds) as the noted term does standing alone. For this reason the instant grounds of rejection has been maintained.

In claim **41** the term "a neurological disorder" is indefinite for failure to particularly point out the specific disease condition to be treated.

Applicant's arguments filed August 1, 2002 have been fully considered but they are not persuasive.

Applicant again relies on disclosure definitions of the noted term, but fails to quote any specific definition. Following an inspection of the disclosure for definitions which might serve to overcome the rejection, examiner found repeated occurrences of the term "e.g." and phrases "pathologies like Alzheimer's disease" wherein the term "like" appears to have been intended to have the same meaning as "e.g." Therefore, examiner fails to agree with applicant that the disclosure provides a proper definition of the noted term. For this reason the instant grounds of rejection has been maintained.

In claims **42 and 50** the term "a memory disorder" is indefinite for failure to particularly point out the specific disease condition to be treated. A similar problem occurs in claim **45** ("memory disorder associated with aging").

Applicant's arguments filed August 1, 2002 have been fully considered but they are not persuasive.

Applicant is referred to the response following the previous rejection.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

> "A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent."

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States."

(e) the invention was described in a patent granted on an application to another filed in the United States before the invention thereof by applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent."

Claims **39, 41-45 and 50** are rejected under 35 U.S.C. §102(**e**) as being anticipated by **Piazza et al. '459** (PTO-892 ref. **B**).

Applicant is referred to claim *1* in the **'759** reference wherein the subject matter claimed includes "treatment of disturbances of the nervous system ... " by "administering ... an effective amount of uridine ... ." Because the claim fails to specify any limit on the dosage size implied by the term "effective amount of uridine," said claim and claims dependent therefrom are deemed to anticipate the instant claims.

Applicant's arguments filed August 1, 2002 have been fully considered but they are not persuasive.

Examiner notes applicant's amendment limiting the administered dosage of "uridine" to "less than 300 mg/day," but also notes that there is no disclosed exemplification which would support this particular limitation (see rejection supra). Therefore, examiner fails to see how applicant can support a change in claim limitations to avoid the noted prior art by limiting dosage, particularly when the claims in said prior art fail to limit the dosage of uridine.

Claims **39, 41-45 and 50** are rejected under 35 U.S.C. §102(**b**) as being anticipated by **Polifarma '267** (PTO-892 ref. **L**)

Applicant is referred to claim ***6*** of the **'267** reference which is directed to pharmaceutical compositions including " ... an amount of uridine therapeutically effective in reducing deficits in neuronal functional activity ... ." Whether this is accomplished by increasing cytidine levels in the brain or is otherwise directly effective is deemed to be impossible to determine. Addressing the specific "increased cytidine level" limitation, examiner finds that administration of uridine to treat any neurological disorder" is likely to increase cytidine levels inherently, even if the report does not specifically report same. This claim limitation appears to read on all levels of uridine administration, including applicant new limitation, and therefore is deemed to anticipate the instant claimed subject matter.

Applicant's arguments filed August 1, 2002 have been fully considered but they are not persuasive.

Examiner notes applicant's amendment limiting the administered dosage of "uridine" to "less than 300 mg/day," but also notes that there is no disclosed exemplification which would support this particular limitation (see rejection supra). Therefore, examiner fails to see how applicant can support a change in claim limitations to avoid the noted prior art by limiting dosage, particularly when the claims in said prior art fail to limit the dosage of uridine.

Claims **39, 41-45 and 50** are rejected under 35 U.S.C. §102(**b**) as being anticipated by **Merlini et al.** (PTO-892 ref. **T**).

Applicant is referred to the abstract supplied, wherein the term "large doses" is not further defined and therefore is deemed to continue to read on the instant claims because the noted doses were effective in improving several mental functions including "memorisation." Whether

this is accomplished by increasing cytidine levels in the brain or is otherwise directly effective is deemed to be impossible to determine. Addressing the specific "increased cytidine level" limitation, examiner finds that administration of uridine to treat any neurological disorder" is likely to increase cytidine levels inherently, even if the report does not specifically report same. Therefore, the instant reference is deemed to read on and therefore anticipate the instant claimed subject matter.

Applicant's arguments filed August 1, 2002 have been fully considered but they are not persuasive.

Applicant is referred to the response following the rejection supra.

Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. §1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. §1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

Papers related to this application may be submitted to Group 1600 via facsimile transmission(FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30,

November 15, 1989). The telephone numbers for the FAX machines operated by Group 1600 are **(703) 308-4556** and **703-305-3592**.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is 703-**308-4639**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson, can be reached at (703)-308-4624.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is 703-**308-1235**.

LECrane:lec
**10/04/02**

Johann Richter, Ph.D., Esq.
Supervisory Patent Examiner
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